REMARKS/ARGUMENTS

At the outset Applicants' representative Heather Morehouse Ettinger would like to thank Examiner Jeffrey Parkin for the telephonic interviews held on May 12, 2005 and March 11, 2005. A brief summary of the May 12, 2005 interview is as follows:

Examiner Parkin notified Dr. Ettinger that the Amendment and Response mailed on March 15, 2005 had been considered and an Advisory Action addressing the response had been mailed out. The Examiner indicated that the Amendment would not be entered because it allegedly raised new issues that would require further consideration and/or searching and allegedly failed to place the application in better form for appeal. Dr. Ettinger was advised that a separate timely filed amendment adopting the changes suggested by the Examiner in the Advisory Action would be entertained.

A brief summary of the March 11, 2005 interview is as follows:

During the interview, the proposed claims faxed to Examiner Parkin for discussion (not for entry in the application) on February 14, 2005 were considered. Examiner Parkin indicated that he and his supervisor had agreed that the claims faxed on February 14, 2005 would be entered and allowed with the following revisions: 1) amending claims 1, 12, 13, 14, 15, 16 and 17 to recite: "wherein β-galactosidase expression is downregulated by the specific binding interaction of the psi sequence with the nucleocapsid protein" and 2) adding the term "only" to the preamble of claim 24 as follows: "[a] microorganism cotransformed with only two plasmid vectors..."

Claim Amendments

Claims 1, 2 and 12-18 have been amended as discussed with the Examiner. Claims 7-8, and 21 have been cancelled, without prejudice or disclaimer. New claims 23 and 24 have been added. Claims 1-3, 12-19, and 22-24 are pending in this application upon entry of this amendment.

Claims 1 and 18 have been amended to recite the phrase "wherein reporter gene expression is downregulated by the specific binding interaction of the psi sequence with the nucleocapsid protein". Claim 18 has also been amended to refer to the phrase "reporter gene expression," rather than β-galactosidase expression because the claim from which claim 18 depends, claim 1, recites "reporter gene expression," not β-galactosidase expression.

Claims 12-17 have been amended to recite "wherein β-galactosidase expression is downregulated by the specific binding interaction of the psi sequence with the nucleocapsid protein."

Support for the amendments set forth above can be found throughout the specification and, in particular, on page 2, line 37 - page 3, line 4; page 4, lines 32-37; page 6, lines 13-25; and Example 3 (page 10, lines 23 - page 16, line 9).

Claims 1, 2, 12, 13, 14, 15, 16 and 17 have been amended to include the word "the" in relation to "HIV nucleocapsid protein" and "HIV psi". These changes were made to correct inadvertent grammatical errors and do not alter the scope of the original claims, *i.e. any* HIV nucleocapsid protein and *any* HIV psi sequence is encompassed by the claim language. Claim 12 has been amended to include "A microrganism comprising" in relation to "*E. coli* JM109". Claims 13, 14 and 15 have been amended to substitute "the" in place of "a" in relation to "vector

pJC1". Claim 18 has been amended to read "A method of screening for" in place of "A method (for) screening". Each of these amendments is made only to correct grammatical mistakes.

Previously presented, now canceled, claims 7 and 8 have been presented as new claims 23 and 24 and their antecedent basis corrected in response to the Examiner's suggestion regarding the order of the claims.

No new matter has been added by way of these claim amendments or new claims.

Rejections Under 35 U.S.C. §103(a)

Claims 1-3, 7, 8, 12-19 and 22 have been rejected as allegedly obvious over Bacharach and Goff (J. Virol. 1998; herein "Bacharach") in view of Strair (Nucleic Acids Res 1993; herein "Strair"). The Examiner again alleges that Bacharach discloses an assay for studying binding interactions between the HIV-1 nucleocapsid (NC) protein and HIV-1 psi (ψ) signal sequence and that the NC protein, target RNA, and reporter gene (β-gal) were expressed from separate plasmids. The Examiner further contends that Strair allegedly discloses a two-plasmid system for identifying antivirals and drug-resistant variants. The Examiner concludes that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the screening assay of Bacharach to include the packaging signal and reporter gene on the same plasmid. The Examiner further alleges that numerous HIV-1 isolates have been sequenced and that selection of any packaging sequence and identification of suitable expression vectors would be a matter of routine experimentation.

This rejection is respectfully traversed. Firstly, nothing in Bacharach or Strair, or the combination of these references, teaches or suggests that reporter gene expression is

downregulated by the specific binding interaction of the psi sequence with the nucleocapsid protein. This feature of the claimed invention is highlighted in claims 1 and 12-17 (and their dependent claims) as currently amended by the phrase "wherein β-galactosidase expression is downregulated by the specific binding interaction of the psi sequence with the nucleocapsid protein" and in claim 18 (and its dependent claims) by addition of the phrase "wherein an increase in reporter gene expression in the presence of the compound or composition compared to reporter gene expression in the absence of the compound or composition indicates the compound or composition inhibits the specific binding interaction between the HIV nucleocapsid protein and the psi sequence." In contrast, in the Bacharach and Strair systems, interaction of the viral protein (e.g. gag or NC) with the psi sequence results in expression, not downregulation, of the lacZ (reporter) gene. Thus, the presently claimed invention, unlike that of Bacharach and Strair, provides a system in which the specific binding interaction of the viral NC protein with psi results in downregulation of reporter (lacZ) gene expression.

Additionally, nothing in Bacharach discloses or suggests that the disclosed three-plasmid system for studying the interaction between the gag protein and psi could be made into a simpler two-plasmid system, as disclosed and claimed in the present application. The Examiner cites Strair for providing a simpler two-plasmid system for developing antivirals. However, Strair does not disclose or suggest a simple two-plasmid system. Rather, Strair discloses a two-step system that is significantly more complicated than the presently claimed invention. Strair discloses a system in which two plasmids are transfected into COS cells to produce an HIV-lacZ virus. This HIV-lacZ virus is then transfected into a target cell and lacZ expression from this second cell is measured. Thus, the Strair system requires use of at least two cell populations and the production of viral particles to get a read-out from the reporter gene (*e.g.* β-galactosidase). In

contrast with the Strair system, the presently claimed invention requires use of only one cell population and does not require the production of viral particles to get a read-out from the reporter gene (*e.g.* β-galactosidase). Thus, nothing in Bacharach or Strair teaches or discloses the simplified two-plasmid system of the present invention.

Furthermore, the system defined by the present claims maintains the specificity of the interaction between the NC protein and the psi sequence, while that of Bacharach does not. This feature of the claimed invention is set forth in claims 1 and 12-18 (and their dependent claims) as currently amended by the phrase "specific binding interaction." Table 3 of Bacharach (on p. 6947 of Bacharach) demonstrates that in their system the specificity of NC-binding to psi is lost. For example, the NC protein of their system is capable of binding to haMSV and IRE. In contrast, the NC protein in the presently claimed system maintains its specificity for the HIV psi sequence (see Example 3 (page 12, lines 2-37 and page 13, lines 1-6) and Figure 3a). The Strair system does not allow for any specificity as the target of the antiviral drugs screened for in Strair is unknown. Thus, the presently claimed microorganism and methods of screening defined by the present claims allow for the interaction between the NC protein and psi to be tested, while the Bacharach or Strair techniques do not.

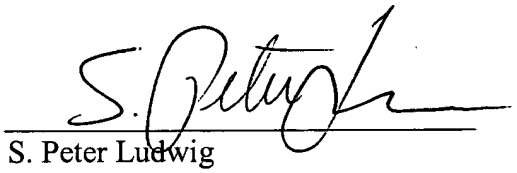
The invention defined by the present claims also provides a more sensitive screening system than that disclosed in Bacharach. Bacharach reports that the level of reporter gene expression is the same when NC or gag is used (see Table 3 of Bacharach). In contrast, the instant application demonstrates that the two-plasmid system results in different levels of reporter gene expression when NC and gag are used (see Example 3 (page 13, lines 7-13) and Figure 3b of the instant application).

In conclusion, nothing in Bacharach or Strair, or the combination of these references, teaches or suggests that reporter gene expression is downregulated by the specific binding interaction of the psi sequence with the nucleocapsid protein. Accordingly, the present invention is not obvious over Bacharach in view of Strair. Moreover, nothing in Bacharach or Strair suggests or discloses the presently claimed two-plasmid system or methods utilizing this two-plasmid system. In addition to being simpler than the Bacharach and Strair systems, the invention defined by the present claims maintains, as discussed above, specificity of the interaction between the NC protein and the psi sequence and provides a more sensitive screening system. Accordingly, nothing in Bacharach or Strair, or the combination thereof, teaches or suggests the claimed invention. Applicants respectfully request withdrawal of the rejection under 35 U.S.C. 103(a).

Conclusion

In view of the above amendments and remarks, reconsideration of this application is respectfully requested. All pending claims should now be in condition for allowance and passage to issue. If there are any other issues remaining which the Examiner believes could be resolved through a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Respectfully submitted,

By: 

S. Peter Ludwig
Reg. No. 25,351
Attorney for Applicants

Dated: July 14, 2005

Darby & Darby P.C.
Post Office Box 5257
New York, NY 10150-5257
212-527-7700